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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,103	12/30/2005	Tore Duvold	3893-0219PUS2	6767
2292 7590 12/24/2008 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747				
EXAMINER				
BADJO, BARBARA P				
ART UNIT		PAPER NUMBER		
1612				
NOTIFICATION DATE		DELIVERY MODE		
12/24/2008		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/563,103

Applicant(s)

DUVOLD ET AL.

Examiner

Barbara P. Badio

Art Unit

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20, 22, 25, 29, 30 and 36 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-20, 22, 25, 29, 30 and 36 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-8508)
Paper No(s)/Mail Date 12/30/2005; 03/09/2007
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

First Office Action on the Merits

Priority

1. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 371, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim

filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Specification

2. The use of the trademark such as "FUCIDIN" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Double Patenting

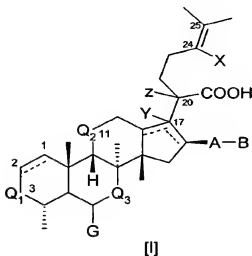
3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-20, 22 and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 of copending Application No. 12/087,743 in view of Olund et al. (US 5,550,145).

Both sets of claims recite compounds of formula I



wherein the variables are as defined therein.

Unlike the instant claims, the claims of the cited application are limited to a topical pharmaceutical composition comprising a monoglyceride of a C₈₋₁₈ fatty acid or a mixture thereof. However, (a) the instant invention is inclusive of pharmaceutical compositions such as topical formulation and (b) Olund teaches the potentiation of the antimicrobial effects of fusidic acid in the presence of monoglyceride of lauric acid or myristic acid (see the entire article, especially col. 2, lines 16-34; Example 4). Therefore, the preparation of a topical formulation comprising the compounds of the instant invention, which are fusidic acid derivatives and a monoglyceride of a fatty acid such as lauric acid or myristic acid, would have been obvious to the skilled artisan in the art at the time of the present invention. The motivation is based on the teaching of the

potentiation of the antimicrobial effect of fusidic acid in the presence of monoglycerides of said fatty acids as taught by Olund.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating or ameliorating bacterial infection, does not reasonably provide enablement for preventing the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not

perform the invention commensurate in scope with the instant claim without undue experimentation.

The instant claim is drawn to a method of treating, preventing or ameliorating bacterial infections by administering the instantly claimed fusidic acid derivatives.

The medical art teaches various treatment regimens for bacterial infections. However, the instant claims recite "preventing," which is deemed to be a "cure" since prevention of a disease is interpreted to mean that the disease will entirely cease to manifest after administration of the composition. Applicant has not demonstrated prevention or curing of any of bacterial infection *in vitro* or even in a mouse/rat model in order to provide some reasonable nexus between the compounds instantly claimed and the prevention of any bacterial infection.

While the Applicants might be enabled for treatment/amelioration **in vitro**, the Applicants are not enabled for curing/preventing any bacterial infection **in vitro** or **in vivo**. The high degree of unpredictability associated with the claimed method underscores the need to provide teachings in the specification that would provide the skilled artisan with specific preventive regimens; however, the present specification does not provide such guidance and fails to provide evidence that the instantly claimed compounds actually prevents or cures any bacterial infection. Without such guidance in the specification and the lack of correlative working examples, the claims would require an undue experimentation without a predictable degree of success on the part of the skilled artisan.

7. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for infections caused by staphylococcus aureus and Streptococcus pyogenes, does not reasonably provide enablement for infections caused by all bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

The instant claim is drawn to a method of treating, preventing or ameliorating bacterial infections by administering the claimed compounds. The present specification provides support by showing the in vitro inhibition of Staph. aureus and Strep. pyogenes (see page 21, line 11 - page 24, line 3).

The state of the pharmaceutical art is such that screening in vitro and in vivo is utilized to determine the desired effect of pharmaceuticals. There is no absolute

predictability of pharmaceuticals and, thus, one of ordinary skill in the art would not accept any therapeutic regimen on its face.

Because the pharmaceutical art is unpredictable, it requires each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d. 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is needed in order to satisfy the statute.

Here, the instantly claimed invention is highly unpredictable because the skilled artisan in the art would recognize the differences in the treatment of the vast array of infections caused by the various known bacteria. Even in the treatment of Staph. infections, the art teaches some strains can be extremely difficult to treat. Therefore, the skilled artisan would doubt a single agent would be effective in treating all Staph. infections and he would especially doubt a single agent would be effective in treating all bacteria infections.

Therefore, in the absence of a showing of correlation between all infections caused by bacteria and the effectiveness of the claimed compounds in treating said infections, one of skill in the art would be unable to fully predict the effect of administration of the said compounds in the treatment of bacteria infections as encompassed by the instant claim.

As stated above, the only guidance given in the present specification is directed to treatment of Staph. Aureus and Strep. pyogenes, which is minimal. Thus, in order to practice the claimed invention commensurate in scope with the instant claim, the skilled

artisan would have to engage in undue experimentation to determine the bacteria infection(s) treatable by the claimed compounds, with no assurance of success.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-20, 22, 25, 29, 30 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite for the following reasons:

(a) The claims recite "B may also represent hydrogen" in several places. The use of the term "may" is unclear because it could imply "B" is other groups not defined by the claims. It is suggested that the term "may" be changed to "is".

(b) The claims recite the phrase "and easily hydrolysable esters". Apart from the specific "easily hydrolysable esters" set forth in the present specification (see page 7, line 35 – page 8, line 4), it is unclear what other esters are encompassed by the phrase.

(c) Claims 16 and 18 recite "-(COH)-" and "the stereochemical configuration is a at both C-3 and C-11". The valence of the carbon atom of the variable "-(COH)-" is incomplete, i.e., the carbon atom has three and not four atoms attached thereto. In addition, the stereochemical configuration recited by the claims is unclear. It is assumed applicant intends "α". Thus, correction is requested.

(d) It is unclear what is intended by the recitation of "Compound #" after each compound in claims 20 and 36. It is suggested that said be deleted.

(e) Claim 20 also recites "a" and "b" within the nomenclature of some of the claimed compounds, for example, 24-bromo-16-deacetoxy-16b-isopropylthio-fusidic acid (Compound 112). It is assumed, applicant intends α or β and, thus, correction is requested.

(f) Claim 20, page 12 recites "with" before the last compound claimed therein, with 24-(trans-1-buten-3,3-dimethyl-1-yl)-fusidic acid pivaloyloxymethyl ester (Compound 307). Did applicant intend the previous compound "with" the above mentioned compound? If not, removal of the term "with" is requested.

(g) Claim 29 recites "a **suitable** fusidic acid analogue in a **suitable** organic solvent.....in a **suitable** solvent in the presence of a **suitable** base...". The term "suitable" implies that there are some fusidic acid analogues, some solvents and some bases that can not utilized in the claimed process. The present specification on pages 26 and 27 discloses analogues, solvents and bases useful in the present process. However, apart from said, it is unclear what other fusidic acid analogue, solvent and base would be suitable.

For these reasons, the skilled artisan would be unable to determine the metes and bound of the claimed invention.

Claim Rejections - 35 USC § 103

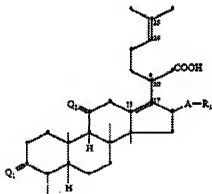
10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

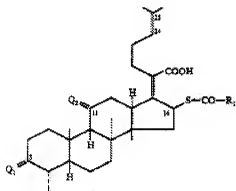
invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1-7, 9, 10, 13-17, 19, 22 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over von Daehne (US 4,100,276 and 4,119,717) and Duvold (US 6,673,783).

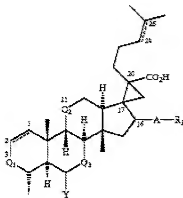
Each of the cited reference teaches derivatives of fusidic acid useful as antibacterial agents (see each reference in its entirety, especially Abstract). Each reference teaches hydrolysable esters such as acetoxymethyl and pivaloyloxymethyl and salts of the prior art compounds (see '276, col. 2, lines 7-32; '717, col. 2, lines 6-24; '783, col. 4, lines 37-55). The derivatives taught by each reference are as follows:



(see '276, col. 1, formula I),



(see '717, col. 1, formula I) and



(see '783, col. 2, formula I).

The instant claims differ from each of the cited reference by reciting the corresponding 24-substituted derivatives, for example, the corresponding 24-methyl derivative of each of the prior art compound. However, hydrogen and methyl are considered obvious variants and, thus, the substitution of hydrogen for methyl on a known compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 USPQ 137. Additional, the steroid art contains numerous teaching of compounds with one carbon difference having similar properties. Therefore, the skilled artisan in the art would have the reasonable expectation that the 24-methyl derivatives of the above cited prior compounds would also be useful antibacterial agents as taught by the references.

Telephone Inquiry

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/
Primary Examiner, Art Unit 1612